Complete Summary

GUIDELINE TITLE

Acute ST-segment elevation myocardial infarction. American College of Chest Physicians evidence-based clinical practice guidelines (8th edition).

BIBLIOGRAPHIC SOURCE(S)

Goodman SG, Menon V, Cannon CP, Steg G, Ohman EM, Harrington RA. Acute ST-segment elevation myocardial infarction: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):708S-75S. [271 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Menon V, Harrington RA, Hochman JS, Cannon CP, Goodman SD, Wilcox RG, Schunemann HJ, Ohman EM. Thrombolysis and adjunctive therapy in acute myocardial infarction: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):549S-75S.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 3, 2008, Innohep (tinzaparin): The U.S. Food and Drug Administration (FDA) has requested that the labeling for Innohep be revised to better describe overall study results which suggest that, when compared to unfractionated heparin, Innohep increases the risk of death for elderly patients (i.e., 70 years of age and older) with renal insufficiency. Healthcare professionals should consider the use of alternative treatments to Innohep when treating elderly patients over 70 years of age with renal insufficiency and deep vein thrombosis (DVT), pulmonary embolism (PE), or both.
- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with

symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.

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SCOPE

DISEASE/CONDITION(S)

ST-segment elevation acute coronary syndromes

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine
Family Practice
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Nurses
Patients
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

To provide evidence-based guidelines on the use of fibrinolytic, antiplatelet, and antithrombin treatment for acute ST-segment elevation (STE) myocardial infarction (MI)

TARGET POPULATION

Patients with ST-segment elevation acute coronary syndromes

INTERVENTIONS AND PRACTICES CONSIDERED

1. Evaluation for reperfusion therapy
2. Fibrinolytic therapy
    - Streptokinase
    - Anistreplase
    - Alteplase
    - Reteplase
    - Tenecteplase
3. Antiplatelet/antithrombotic therapy
    - Aspirin
    - Clopidogrel
4. Antithrombin therapy
    - Unfractionated heparin (UFH)
    - Low molecular weight heparin (LMWH)
    - Fondaparinux
5. Glycoprotein (GP) IIb/IIIa inhibitors
    - Abciximab
6. Rescue percutaneous coronary intervention (PCI)
7. Monitoring
    - Activated clotting time (ACT)
    - Activated partial thromboplastin time (APTT)

MAJOR OUTCOMES CONSIDERED

- Mortality
- Incidence of thrombosis
- Incidence of major and minor hemorrhage
- Recurrent myocardial infarction
- Incidence of intracranial hemorrhage

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Process of Searching for Evidence

Defining the clinical question provided the framework for formulating eligibility criteria that guided the search for relevant evidence. In specifying eligibility criteria, authors identified not only patients, interventions, and outcomes, but also methodologic criteria. For many recommendations, authors restricted eligibility to randomized controlled trials (RCTs).

For many questions, randomized trials did not provide sufficient data, and chapter authors included observational studies when randomized trials were not the most appropriate design to address the research question. In particular, randomized trials are not necessarily the best design to understand risk groups, that is, the baseline or expected risk of a given event for certain subpopulations. Because no interventions are typically examined in questions about prognosis, one replaces interventions by the duration of exposure measured in time.

Identifying the Evidence

To identify the relevant evidence, a team of librarians and research associates at the McMaster University Evidence based practice center (EPC) conducted comprehensive literature searches. Methodologic experts (including the editors) and the EPC librarians reviewed each question to ensure the development of a comprehensive search strategy. For example, for questions about antiplatelet agents, the EPC consulted chapter authors to ensure that the search included all relevant antiplatelet agents. More specifically, authors then decided whether to include dipyridamole in a search that already included aspirin, clopidogrel, and ticlopidine.

For each question the authors provided, the librarians searched the Cochrane Database of Systematic Reviews, MEDLINE, and Embase for published English-language literature and human studies between 2002 and May 2006. To filter MEDLINE and Embase search results for RCT evidence, the librarians used the search strategy developed by the Cochrane Collaboration. These searches updated the more comprehensive and sensitive searches conducted for the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence Based Guidelines.

The EPC team conducted separate searches for systematic reviews; RCTs; and, if applicable, observational studies. For observational studies, searches were not restricted in terms of methodology. Although increasing the probability of identifying all published studies, this sensitive approach resulted in large numbers of citations for many of the defined clinical questions. Therefore, trained research assistants screened the citation list developed from the search using criteria of increased specificity to reduce the number of irrelevant citations that the authors received. These irrelevant citations included press news, editorials, narrative reviews, single-case reports, studies that included fewer participants than specified by authors as an inclusion criterion, animal studies (any nonhuman studies), and letters to the editor. Authors did not include data from abstracts of meetings for the development of recommendations, and the guideline developers did not explicitly use Internet sources to search for research data. Authors were encouraged, however, to mention abstracts that reported on groundbreaking data that were particularly relevant to a specific question in the chapters in order to alert readers that new, fully published evidence might become available shortly.

Standard Consideration of Study Quality

High-quality clinical guidelines should pay careful attention to the methodologic quality of the studies that form the basis of their recommendations. Using the example of the prevention of venous thromboembolism during air travel, Table 1 in the methodology companion (see "Availability of Companion Documents" field) shows the criteria for assessment of study quality (randomization, concealment or treatment allocation, blinding, completeness of follow-up, and whether the analysis was performed according to the intention-to-treat principle), and Table 2 in the methodology companion (see "Availability of Companion Documents" field) shows the presentation of results that were circulated to the authors. Whereas all authors attended to these criteria, the guideline developers have summarized the results of the quality assessment for only a minority of the recommendations. Readers can find these summaries in an online appendix to the recommendations (see online supplemental data).

In assessing the quality of observational studies, the guideline developers did not make a distinction between prospective and retrospective because the key issues are unbiased sampling, high-quality measurement of patient characteristics and outcomes, and complete follow-up.

Although it is more likely that these quality criteria will be achieved in prospective studies, prospective studies may fail to achieve them, and retrospective studies may succeed. The guideline developers did make a key distinction about whether internal comparisons exist and their nature. Studies without internal comparisons received the label "case series" unless they met the following criteria: (1) a protocol existed before the date of commencement of data collection; (2) a definition of inclusion and exclusion criteria was available; (3) the study reported the number of excluded patients; (4) the study conducted a standardized follow-up, including description of schedule of follow-up, investigation of suspected outcomes, and criteria used to define outcomes; and (5) the study reported all losses to follow-up.

The guideline developers labeled studies that met these criteria "cohort studies without internal controls." Studies with internal comparisons received the label "cohort studies with concurrent controls" or "cohort studies with historical controls." These cohort studies may succeed or fail to ensure settings, similar time frames, adjustment for differences in patients' characteristics, and follow-up with patients. These features were captured in descriptive tables provided to authors when requested from the EPC.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) and the methodological quality of the underlying evidence (A, B, or C). See "Grades of recommendations for antithrombotic agents" in the "Availability of Companion Documents" field and the "Rating Scheme for the Strength of the Recommendations." field.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Summarizing Evidence

The electronic searches also included searches for systematic reviews. If authors were satisfied with a recent high-quality systematic review, evidence from that review provided a foundation for the relevant recommendation.

Pooled analyses from high-quality systematic reviews formed summary data on which panelists based their recommendations wherever possible. Pooling offers the advantage of obtaining more precise estimates of treatment effects and allows for greater generalizability of results. However, pooling also bears the risk of spurious generalization. In general, the summary estimates of interest were the different types of outcomes conveying benefits and downsides (risk, burden, and cost). When pooled estimates of effects were not available, the McMaster University Evidence based practice center (EPC) conducted meta-analysis to obtain pooled estimates for specific questions. These were questions that authors had specifically identified.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Group-Specific Recommendations

In general, the guideline developers have endeavored to make their recommendations as specific as possible for patient subgroups differing according to risk. Whenever valid prognostic data were available, the guideline developers used them to estimate absolute effects and made recommendations accordingly. Unfortunately, reliable prognostic indexes are not usually available, limiting the extent to which such group-specific recommendations are possible.

Acknowledge Values and Preferences and Resource Use Underlying Recommendations

Under ideal circumstances, knowledge of average patient values and preferences would be available for every recommendation, the panel members would

summarize these values and preferences, and they would be integrated into the recommendations that guideline developers make. The guideline developers asked all chapter chairs before beginning the searches for the relevant literature to identify recommendations that they believed were particularly sensitive to patients' values and preferences. Moderate-quality evidence regarding values and preferences bearing directly on the recommendations proved available for only the chapter that addresses antithrombotic therapy in patients with atrial fibrillation. The panelists bore in mind what average patient values and preferences may be; the process, however, is speculative.

The guideline developer's main strategy for dealing with this unsatisfactory situation is to make the values and preferences underlying the recommendations explicit whenever the panelists believed that value and preference issues were crucial for a recommendation.

In addition, the guideline developers involved three consultants with expertise in the area of values and preferences to collaborate with the chairs of two chapters and try to ensure that the guidelines adequately represented the views of patients. This collaboration led to extensive discussions among the chapter authors and the consultants and the reflection of these discussions in the associated values and preference statements.

Finalizing and Harmonizing Recommendations

After having completed the steps the guideline developers have described above, the guideline authors formulated draft recommendations before the conference, which laid the foundation for authors to work together and critique the recommendations. Figure 1 in the methodology companion (see "Availability of Companion Documents" field) shows the process of guideline development and review. Drafts of chapters that included draft recommendations were usually distributed for peer review to at least two panel members and were always reviewed by at least one panel editor before the conference. Written critiques were prepared and returned to the authors for revision of their work. At the plenary conference, a representative of each chapter presented potentially controversial issues in their recommendations. Chapter authors met to integrate feedback and consider related recommendations in other chapters and to revise their own guidelines accordingly. Authors continued this process after the conference until they reached agreement within their groups and with other author groups who provided critical feedback. The editors of this supplement harmonized the chapters and resolved remaining disagreements between chapters through facilitated discussion. All major correspondence and discussions at the meeting were recorded in written and audio protocols and are publicly available.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading Recommendation

Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; higher quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation, low or very low-quality evidence, Grade 1C	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient or society values; further research is very unlikely to change our confidence in the estimate of effect
Weak recommendation, moderate-quality evidence, Grade 2B	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very	Best action may differ depending on circumstances or patient or society values; higher-quality research may well have an important impact on our confidence in the

Grading Recommendation			
Grade of Recommendation*	**Benefit vs. Risk and Burdens**	**Methodologic Quality of Supporting Evidence**	**Implications**
		strong evidence from observational studies	estimate of effect and may change the estimate
Weak recommendation, low or very low-quality evidence, Grade 2C	Desirable effects closely balanced with undesirable effects	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

*The guideline developers use the wording *recommend* for strong (Grade 1) recommendations and *suggest* for weak (Grade 2) recommendations.

COST ANALYSIS

For these guidelines, the guideline developers implemented recommendations of a recent American College of Chest Physicians (ACCP) task force on integrating resource allocation in clinical practice guidelines by restricting resource expenditure consideration to a small number of recommendations for which they were particularly relevant. The guideline developers relied on two consultants with expertise in economic assessment to help with the process of considering costs in those small numbers of recommendations that the guideline developers considered very important to the decision.

Recommendations highly sensitive to resource allocation now include value and preference statements regarding how cost issues were integrated.

Refer to "Strategies for incorporating resource allocation and economic considerations" (see "Availability of Companion Documents" field) for details of the cost analyses.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The American College of Chest Physicians (ACCP) Health Science Policy (HSP) established a process for the thorough review of all ACCP evidence-based clinical practice guidelines. After final review by the editors, the guidelines underwent

review by appropriate NetWorks of the ACCP (for these guidelines, the Cardiovascular and Pulmonary Vascular NetWorks), the HSP, and the Board of Regents. The latter two have the right of approval or disapproval but usually work with the guideline authors and editors to make necessary revisions before final approval. Each group identified primary reviewers who read the full set of chapters as well as individual committee members who were responsible for reviewing one or more chapters. The reviewers considered both content and methodology as well as whether there was balanced, not biased, reporting and adherence to HSP processes. Finally, the *CHEST* editor-in-chief read and forwarded the manuscripts for nonbiased, independent, external peer review before acceptance for publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The grades of recommendation (1A, 1B, 1C, 2A, 2B, 2C) are defined at the end of the "Major Recommendations" field.

Reperfusion Therapy

For patients with ischemic symptoms characteristic of acute myocardial infarction (MI) of $\leq$ 12 hours duration and persistent ST-segment elevation (STE), the guideline developers recommend that all undergo rapid evaluation for reperfusion (primary percutaneous coronary intervention [PCI] or fibrinolytic) therapy and have a reperfusion strategy implemented promptly after contact with the health-care system **(Grade 1A)**.

Fibrinolysis

1. In patients with acute MI who are candidates for fibrinolytic therapy, the guideline developers recommend administration as soon as possible (ideally within 30 min) after arrival to the hospital or first contact with the health-care system **(Grade 1A)**.
2. In health-care settings where prehospital administration of fibrinolytic therapy is feasible, the guideline developers recommend prehospital administration of fibrinolytic therapy **(Grade 1A)**.
3. For patients with ischemic symptoms characteristic of acute MI of $\leq$ 12 hours duration, and persistent STE, the guideline developers recommend administration of streptokinase, anistreplase, alteplase, reteplase, or tenecteplase over no fibrinolytic therapy **(all Grade 1A)**.
4. For patients with symptom duration $\leq$ 6 hours, the guideline developers recommend the administration of alteplase **(Grade 1A)** or tenecteplase **(Grade 1A)**, and suggest reteplase **(Grade 2B)** over streptokinase.
5. For patients receiving fibrinolytic therapy, the guideline developers suggest the use of a bolus agent (e.g., tenecteplase) to facilitate the ease of administration and potentially reduce the risk of nonintracranial hemorrhage (ICH)-related bleeding (tenecteplase) **(Grade 2A)**.
6. For patients with ischemic symptoms characteristic of acute MI of $\leq$ 12 hours duration, and left bundle-branch block (BBB) with associated STE changes,

the guideline developers recommend fibrinolytic therapy if primary percutaneous coronary intervention (PCI) is not readily available **(Grade 1B)**.

7. For patients with ischemic symptoms characteristic of acute MI of ≤ 12 hours duration and ECG findings consistent with a true posterior MI, the guideline developers suggest fibrinolytic therapy if primary PCI is not readily available **(Grade 2B)**.
8. For high-risk patients with ongoing symptoms characteristic of acute MI or hemodynamic compromise and duration of 12 to 24 hours who have persistent STE or left BBB with STE changes, the guideline developers suggest fibrinolytic therapy if primary PCI is not readily available **(Grade 2B)**.
9. In patients with any history of intracranial hemorrhage (ICH), or with history of head trauma, or with ischemic stroke within the past 6 months, the guideline developers recommend against administration of fibrinolytic therapy **(Grade 1C)**.

Antiplatelet/Antithrombotic Therapy

Aspirin

For patients with acute STE MI, whether or not they receive fibrinolytic therapy, the guideline developers recommend aspirin (160 to 325 mg orally [po]) over no aspirin therapy at initial evaluation by health-care personnel **(Grade 1A)** followed by indefinite therapy (75 to 162 mg/d po) **(Grade 1A)**.

Clopidogrel

1. For patients with acute STE MI, the guideline developers recommend clopidogrel in addition to aspirin **(Grade 1A)**. The recommended dosing for clopidogrel is 300 mg po for patients ≤ 75 years old and 75 mg po for patients age > 75 years if they receive fibrinolytic agents or no reperfusion therapy, followed by 75 mg/d po for up to 28 days **(Grade 1A)**.
2. For patients with acute STE, MI who have not received a coronary stent, the guideline developers suggest that clopidogrel 75 mg/d could be continued beyond 28 days and up to 1 year **(Grade 2B)**.
3. For patients undergoing primary PCI, the guideline developers suggest clopidogrel in addition to aspirin with a recommended initial dosing of at least 300 mg **(Grade 1B)**, followed by 75 mg daily (for duration of therapy, see the National Guideline Clearinghouse (NGC) summary of the American College of Chest Physician (ACCP) chapter The primary and secondary prevention of coronary artery disease by Becker et al.)

Antithrombin Therapy

For patients with acute STE MI, in addition to aspirin and other antiplatelet therapies, the guideline developers recommend the use of antithrombin therapy over no antithrombin therapy **(Grade 1A)**, including for those patients receiving fibrinolysis (and regardless of which lytic agent is administered), primary PCI, or patients not receiving reperfusion therapy.

Unfractionated Heparin (UFH)

1. For patients receiving streptokinase, the guideline developers suggest administration of either intravenous (IV) UFH (5,000-U bolus followed by 1,000 U/hour for patients > 80 kg, 800 U/hour for < 80 kg) with a target activated partial thromboplastin time (APTT) of 50 to 75 seconds or subcutaneous (SC) UFH (12,500 U every (q) 12 hours) over no unfractionated heparin (UFH) therapy for 48 hours **(both Grade 1B)**.
2. For patients receiving alteplase, tenecteplase, or reteplase for fibrinolysis in acute MI, the guideline developers recommend administration of weight-adjusted heparin (60 U/kg bolus for a maximum of 4,000 U followed by 12 U/kg/hour [1,000 U/hour maximum]) adjusted to maintain an APTT 50 to 70 seconds for 48 hours **(Grade 1B)**.
3. For patients with STE MI undergoing primary PCI, the guideline developers recommend administration of IV UFH over no UFH therapy **(Grade 1C)**. The recommended periprocedural dosing in patients receiving a glycoprotein (GP) IIb/IIIa inhibitor is 50 to 70 U/kg (target activated clotting time [ACT] > 200 seconds); in patients not receiving a GP IIb/IIIa inhibitor, the recommended periprocedural dosing is 60 to 100 U/kg (target activated clotting time, 250 to 350 seconds).

Low-Molecular Weight Heparin (LMWH)

1. For patients with acute STE MI, regardless of whether or not they receive reperfusion therapy, the guideline developers recommend the use of reviparin over no therapy **(Grade 1B)**. Recommended dosing for reviparin is 3,436 IU for < 50 kg, 5,153 IU for 50 to 75 kg, or 6,871 IU for > 75 kg q 12 hours SC up to 7 days. For patients undergoing primary PCI, UFH should be used periprocedurally and reviparin initiated 1 hour after sheath removal.
2. For patients with acute STE MI receiving fibrinolytic therapy who have preserved renal function (> 2.5 mg/dL [220 micromol/L] in male patients and < 2.0 md/dL [175 micromol /L] in female patients), the guideline developers recommend the use of enoxaparin over UFH, continued up to 8 days **(Grade 2A)**. Recommended dosing for enoxaparin is for age < 75 years, 30 mg IV bolus followed by 1 mg/kg SC q 12 hours (maximum 100 mg for the first two SC doses); and for age $\geq$ 75 years, no IV bolus, 0.75 mg/kg SC q 12 hours (maximum, 75 mg for the first two SC doses).

Fondaparinux

1. For patients with acute STE MI and not receiving reperfusion therapy, the guideline developers recommend fondaparinux over no therapy **(Grade 1A)**. Recommended dosing for fondaparinux is 2.5 mg IV for the first dose and then SC once daily (qd) up to 9 days.
2. For patients with acute STE MI receiving fibrinolytic therapy and thought not to have an indication for anticoagulation, the guideline developers recommend fondaparinux over no therapy (2.5 mg IV for the first dose and then SC qd up to 9 days) **(Grade 1B)**.
3. For patients with acute STE MI receiving fibrinolytic therapy and thought to have an indication for anticoagulation, the guideline developers suggest fondaparinux (2.5 mg IV for the first dose and then SC qd up to 9 days) could be used as an alternative to UFH **(Grade 2B)**.
4. For patients with acute STE MI and undergoing primary PCI, the guideline developers recommend against using fondaparinux **(Grade 1A)**.

Direct Thrombin Inhibitors

For patients with acute STE MI treated with streptokinase, the guideline developers suggest clinicians not use bivalirudin as an alternative to UFH **(Grade 2B)**.

Underlying values and preferences: This recommendation places a relatively higher value on avoiding excess of major bleeding and a relatively lower value on avoiding reinfarction. Recommended dosing for bivalirudin is 0.25 mg/kg IV bolus followed by an infusion of 0.5 mg/kg/h for the first 12 hours and then 0.25 mg/kg/h for the subsequent 36 hours; APTTs should be measured at 12 hours and 24 hours with potential dose reductions as noted (see text above).

GP IIb/IIIa Inhibitors

1. For patients with acute STE MI, the guideline developers recommend against the combination of standard-dose abciximab and half-dose reteplase or tenecteplase with low-dose IV UFH over standard-dose reteplase or tenecteplase **(Grade 1B)**.
2. For patients with acute STE MI, the guideline developers suggest clinicians not use the combination of streptokinase and any GP IIb/IIIa inhibitor **(Grade 2B)**.
3. For patients with acute STE MI undergoing primary PCI (with or without stenting), the guideline developers recommend the use of abciximab **(Grade 1B)**. Recommended dosing for abciximab is 0.25 mg/kg IV bolus followed by 0.125 micrograms/kg/min (maximum, 10 micrograms/min) for 12 hours.

Facilitated PCI

1. For patients with acute STE MI undergoing primary PCI, the guideline developers recommend against the use of fibrinolysis, with or without a GP IIb/IIIa inhibitor **(Grade 1B)**.
2. For patients with acute STE MI who are to undergo primary PCI, the guideline developers suggest administration of a GP IIb/IIIa inhibitor prior to coronary angiography **(Grade 2B)**. The largest number of patients studied in this setting received abciximab 0.25 mg/kg IV bolus followed by 0.125 micrograms/kg/min (maximum 10 micrograms/min) for 12 hours; recommended dosing for eptifibatide is two 180 microgram IV boluses (10 min apart) followed by 2.0 micrograms/kg/min infusion for 12–24 hours; recommended dosing for tirofiban is 25 micrograms/kg IV bolus followed by 0.15 micrograms/kg/min for 24 hours.

Rescue PCI

For patients with STE MI who have received fibrinolysis but who have persistent STE (< 50% resolution 90 min after treatment initiation compared with the pretreatment electrocardiogram [ECG]), the guideline developers recommend rescue PCI should be performed over repeat fibrinolysis or no additional reperfusion therapy **(Grade 1B)**, and suggest as soon as possible and within 2 hours of identification of lack of STE resolution **(Grade 2C)**.

Definitions:

Grading Recommendation			
Grade of Recommendation*	**Benefit vs. Risk and Burdens**	**Methodologic Quality of Supporting Evidence**	**Implications**
Strong recommendation, high-quality evidence, Grade 1A	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; higher quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation, low or very low-quality evidence, Grade 1C	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient or society values; further research is very unlikely to change our confidence in the estimate of effect
Weak recommendation, moderate-quality evidence, Grade 2B	Desirable effects closely balanced with	Evidence from RCTs with important limitations (inconsistent results,	Best action may differ depending on circumstances or patient or society values; higher-quality research

Grading Recommendation			
Grade of Recommendation*	**Benefit vs. Risk and Burdens**	**Methodologic Quality of Supporting Evidence**	**Implications**
	undesirable effects	methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	may well have an important impact on our confidence in the estimate of effect and may change the estimate
Weak recommendation, low or very low-quality evidence, Grade 2C	Desirable effects closely balanced with undesirable effects	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

*The guideline developers use the wording *recommend* for strong (Grade 1) recommendations and *suggest* for weak (Grade 2) recommendations.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate fibrinolytic, antiplatelet, and antithrombin treatment of patients with ST-segment elevation acute coronary syndromes

POTENTIAL HARMS

Fibrinolytic, antiplatelet, and antithrombin treatment may be associated with an increased risk of hemorrhagic events

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications and Cautions for Fibrinolysis in ST-segment Elevation Myocardial Infarction (STEMI)

Absolute Contraindications

- Any prior intracranial hemorrhage (ICH)
- Known structural cerebral vascular lesion (e.g., arteriovenous malformation)
- Known malignant intracranial neoplasm (primary or metastatic)
- Ischemic stroke within 3 months except acute ischemic stroke within 3 hours
- Suspected aortic dissection
- Active bleeding or bleeding diathesis (excluding menses)
- Significant closed-head or facial trauma within 3 months

Relative Contraindications

- History of chronic, severe, poorly controlled hypertension
- Severe uncontrolled hypertension on presentation (systolic blood pressure [BP] >180 mm Hg or diastolic BP >110 mm Hg)
- History of prior ischemic stroke > 3 months, dementia, or known intracranial pathology not covered in contraindications
- Traumatic or prolonged (>10 min) cardiopulmonary resuscitation or major surgery (≤3 wk)
- Recent (≤ 2–4 wk) internal bleeding
- Noncompressible vascular punctures
- For streptokinase/anistreplase: prior exposure (>5 days ago) or prior allergic reaction to these agents
- Pregnancy
- Active peptic ulcer
- Current use of vitamin K antagonists: the higher the international normalized ratio (INR), the higher the risk of bleeding

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Limitations of These Guideline Development Methods

Limitations of these guidelines include the limited quantity and quality of available studies for some patient groups. Second, it is possible that some authors followed this methodology more closely than others, although the development process was centralized by an evidence-based practice center (EPC) and supervised by the editors. Third, it is possible that the guideline developers missed relevant studies in spite of the comprehensive searching process. Fourth, despite their efforts to begin centralizing the methodologic evaluation of all studies to facilitate uniformity in the validity assessments of the research incorporated into these guidelines, resources were insufficient to conduct this evaluation for all but a few of the

recommendations in each chapter. Fifth, the guideline developers performed only few statistical pooling exercises of primary study results. Finally, sparse data on patient preferences and values represent additional limitations inherent to most guideline development methods.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy includes local educational programs and tools offered through the American College of Chest Physicians (ACCP) Board of Governors and select other locations. The Veterans Administration (VA) will also participate in a pilot project.

IMPLEMENTATION TOOLS

Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Goodman SG, Menon V, Cannon CP, Steg G, Ohman EM, Harrington RA. Acute ST-segment elevation myocardial infarction: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):708S-75S. [271 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Jan (revised 2008 Jun)

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Chest Physicians

GUIDELINE COMMITTEE

American College of Chest Physicians (ACCP) Expert Panel on Antithrombotic and Thrombolytic Therapy

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr. Goodman discloses that he has received grant monies from Biovail, Bristol-Myers Squibb, GlaxoSmithKline, Hoffman- La Roche, Lilly, Merck, Sanofi-Aventis, Schering, and The Medicines Company. He has also received consultant fees from Bristol-Myers Squibb, GlaxoSmithKline, Hoffman-La Roche, Lilly, Sanofi-Aventis, and The Medicines Company.

Dr. Menon discloses that he is on the speakers bureau for Roche and Datascope, and that he has served on an advisory committee for Roche.

Dr. Cannon discloses that he has received grant monies from Accumetrics, AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Merck, Sanofi-Aventis, and Schering Plough.

Dr. Ohman discloses that he has received grant support from Bristol-Myers Squibb, Sanofi-Aventis, Schering-Plough, Millenium Pharmaceuticals, Eli Lilly, and Berlex. He has received consultant fees from Inovise, Savacor, Liposcience, Response Biomedical, The Medicines Company, Datascope, and Abiomed, and is on the speakers bureaus for CV Therapeutics and Schering- Plough. Dr. Ohman is also a shareholder of Inovise, Savacor, and Medtronic.

Dr. Steg discloses that he has received grant monies from Sanofi-Aventis, and consultant fees from Sanofi-Aventis, Astra-Zeneca, BMS, Boehringer-Ingelheim, Takeda, Amgmeo, Thermedicine, MSD, GSK, and Servier. He has served on the speakers bureau at Sanofi-Aventis, AstraZeneca, BMS, Boehringer-Ingelheim, Takeda, Amgen, Thermedicine, MSD, GlaxoSmithKline, and Servier.

Dr. Harrington discloses that he holds a fiduciary position as Director of the Duke Clinical Research Institute (DCRI). Either he or the DCRI have received grant monies from the following: Abbott Laboratories; Abbott Vascular Business; Acorn Cardiovascular; Actelion, Ltd; Acusphere, Inc; Adolor Corporation; Advanced Cardiovascular Systems, Inc; Air Products; PLC; Ajinomoto; Alexion, Inc; Allergan, Inc; Alsius Corporation; Amgen, Inc; Amylin Pharmaceuticals; Anadys; Angel Medical Systems, Inc; AnGes MG Inc; Angiometrx, Inc; ArgiNox Pharmaceuticals; Ark Therapeutics; Astellas Pharma US; Astra Hassle; AstraZeneca; Atritech; Aventis; BARRX Medical, Inc; Baxter; Bayer AG; Bayer Corporation US; Berlex, Inc; Bioheart; Biolex Therapeutics; Biosense Webster, Inc; Biosite, Inc (also Biosite Diagnostics); Biosysnexus; Boehringer Ingelheim; Boston MedTech Advisors; Bristol Scientific Corporation; Bristol-Myers Squibb; CanAm Bioresearch; Cardio Thoracic Systems; CardioDynamics International; CardioKinetix; CardioOptics; Celgene Corporation; Celsion Corporation; Centocor; Cerexa, Inc; Chase Medical; Chugai Pharmaceutical; Cierra Inc; Coley Pharmaceutical Group; Conor Medsystems; Corautus Genetics; Cordis; Critical Therapeutics; Cubist Pharmaceuticals; CV Therapeutics; Cytokinetics; Daiichi Sankyo; deCode Genetics; Dyax; Echosens, Inc; Eclipse Surgical Technologies; Edwards Lifesciences; Eli Lilly & Company; EnteroMedics; Enzon Pharmaceutical; EOS Electro Optical Systems; EPI-Q, Inc; ev3, Inc; Evalve, Inc; Flow Cardia Inc; Fox Hollow Pharmaceuticals; Fujisawa; Genentech; General Electric Company; General Electric Healthcare; General Electric Medical Systems; Genzyme Corporation; Getz Bros & Co, Inc; GlaxoSmithKline; Globelmmune; Gloucester Pharmaceuticals; Guidant Pharmaceuticals; Heartscape Technologies; Hoffmann-

LaRoche; Human Genome Sciences, Inc; ICAGEN; iCo Therapeutics; IDB Medical; Idenix Pharmaceutical; Indigo Pharmaceutical; INFORMD, Inc; InfraReDx; Inhibitex; Innocoll Pharmaceuticals; Inspire Pharmaceuticals; Intarcia Therapeutics; Integrated Therapeutics Group; Inverness Medical Innovations; Ischemix, Inc; Johnson & Johnson; Jomed, Inc; KAI Pharmaceuticals; Kerberos Proximal Solutions, Inc; Kinetic Concepts, Inc; King Pharmaceuticals; Kuhera Chemical Co; Lilly; Lumen Biomedical, Inc; Medical Educations Solutions Group; Medicure International; MiniMed; Medi-Flex, Inc; MedImmune; Medtronic AVE; Medtronic Diabetes; Medtronic, Inc; Medtronic Vascular; Merck Group; Microphage, Inc; Millennium Pharmaceutical; Mosby; Mycosol, Inc; NABI Biopharma; Neuron Pharmaceuticals; NicOx; NitroMed; NovaCardia Inc; Novartis AG Group; Novartis Pharmaceuticals; OLG Research; Ortho Biotech; OSI Eyetech; Osiris Therapeutics; Otsuka Pharmaceutical; Pathway Medical Technologies; PDL bio Pharma; PDxRx, Inc; Peregrine Pharmaceuticals; Pfizer; Pharmacyclics; Pharmanetics; Pharmassest; Pharsight, Inc; Portola Pharmaceutical; Proctor & Gamble; Radiant; Reata Pharmaceuticals; Recom Managed Systems, Inc; Regado Biosciences; Reliant Pharmaceuticals; Roche Diagnostic Corp; Salix Pharmaceuticals; Sanofi Pasteur, Inc (formerly Aventis-Pasteur); Sanofi-Aventis; Sanofi- Synthelabo; Schering-Plough Corporation; SciClone Pharmaceuticals; Scios; Seredigm; Sicel Technologies; Siemens; Skyline Ventures; Social Scientific Solutions; Spectranetics; Summit; Suneis; TAP Pharmaceutical Products; Tengion; Terumo Corporation; The Medicines Company; Theravance; TherOx, Inc; Thoratec Corporation; Titan Pharmaceuticals; United Therapeutics; Uptake Medical Corporation; Valleylab; Valeant Pharmaceuticals International; Valentis, Inc; Vascular Solutions, Inc; Velocimen, Inc; Veridex; Vertex Pharmaceuticals; VIASYS Healthcare; Vicuron Pharmaceuticals (formerly Versicor); ViroChem Pharma, Inc; Watson Pharmaceuticals; WebMD; Wyeth; Xsira Pharmaceuticals (formerly Norak Biosciences); and/or XTL Biopharma.

ENDORSER(S)

American College of Clinical Pharmacy - Medical Specialty Society
American Society of Health-System Pharmacists - Professional Association

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Menon V, Harrington RA, Hochman JS, Cannon CP, Goodman SD, Wilcox RG, Schunemann HJ, Ohman EM. Thrombolysis and adjunctive therapy in acute myocardial infarction: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):549S-75S.

GUIDELINE AVAILABILITY

Electronic copies: Available to subscribers of the Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

Executive Summary:

- Antithrombotic and thrombolytic therapy executive summary. Chest 2008 Jun; 133:71S-109S.

Background Articles:

- Antithrombotic and thrombolytic therapy. Chest 2008 Jun; 133:110S-112S.
- Methodology for antithrombotic and thrombolytic therapy guideline development. Chest 2008 Jun; 133:113S-122S.
- Grades of recommendation for antithrombotic agents. Chest 2008 Jun; 133:123S-131S.
- Strategies for incorporating resource allocation and economic considerations. Chest 2008 Jun; 133:132S-140S.

Electronic copies: Available to subscribers of the Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on July 30, 2001. The information was verified by the guideline developer on October 17, 2001. This NGC summary was updated by ECRI on December 9, 2004. The updated information was verified by the guideline developer on January 12, 2005. This summary was updated by ECRI Institute on June 22, 2007 following the U.S. Food and Drug Administration (FDA) advisory on heparin sodium injection. This summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection. This NGC summary was completed by ECRI Institute on December 8, 2008. The updated information was verified by the guideline developer on January 7, 2009.

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Date Modified: 2/16/2009